CLAIMS

1. A peptide of structure CM-R_3-$(CA)_n$-AA_1-AA_2-AA_3-AA_4-AA_5-AA_6-OH, wherein said peptide has a selective affinity for neurotensin receptors and wherein

CM is a chelating moiety or metal binding site;

R_3 is D-lysine, D-phenylalanine, any D-amino acid, glycine-glycine-glycine, Gly-Ser-Gly, Tyr-Glu-Asn, DTyr-Glu-Asn, Phe-Glu-Asn, DPhe-Glu-Asn, piperidinyl glycine, aminomethylcyclohexylalanine, amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or an alkyl amino substituent either externally or as a part of the ring, or a spacer unit;

CA is a cyclic amino acid selected from the group consisting of proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, and other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or an alkyl amino substituent either externally or as a part of the ring;

n = 0, 1 or 2;

AA_1 is an amino acid which comprises a guanidino group and wherein the α-carbon is either L- or D-, with the proviso that AA_1 is not arginine;

AA_2 is arginine, lysine, piperidinylglycine, or other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the α-carbon, or AA_2 is an amino acid which comprises a guanidino group wherein the α-carbon is either L- or D-;

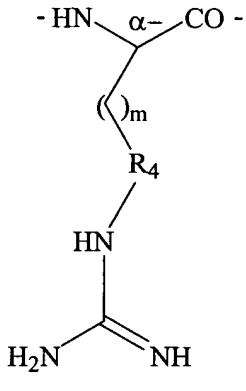
AA_3 is a cyclic amino acid selected from proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, or other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the α-carbon;

AA_4 is phenylalanine, tyrosine, an isomer of tyrosine, polyhydroxylated phenylalanine, or other aromatic amino acid, wherein the amino acid can have the L- or D-configuration at the α-carbon;

AA_5 is isoleucine; and

AA_6 is leucine.

2. The peptide of claim 1 wherein AA_1 is



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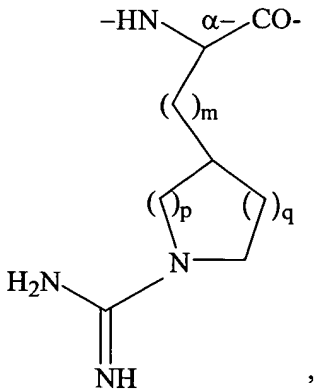

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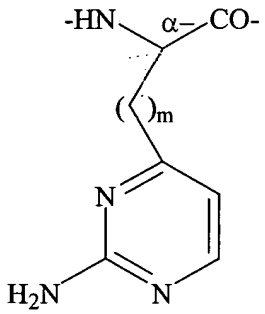

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wherein

m = 0-6;

p = 1-7;

q = 1-7; and

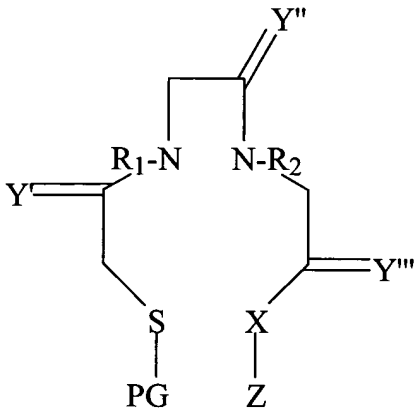
R_4 is cycloalkyl C_3-C_{10}, phenyl, aralkyl, substituted phenyl or substituted aralkyl comprising an electron withdrawing or electron donating group with the proviso that said guanidino group is at a position different from said electron withdrawing or electron donating group.

3. The peptide of claim 1 wherein said peptide is labeled with a radioisotope.

4. The peptide of claim 3 wherein said label is ^{99m}Tc, ^{203}Pb, ^{67}Ga, ^{111}In, ^{97}Ru, ^{62}Cu, ^{64}Cu, ^{186}Re, ^{188}Re, ^{90}Y, ^{121}Sn, ^{161}Tb, ^{153}Sm, ^{166}Ho, ^{105}Rh, ^{177}Lu or a radioactive halogen isotope.

5. The peptide of claim 4 wherein if said label is a metal then CM is a chelating group for said metal and if said label is a halogen then said halogen is bound to an aromatic ring.

6. The peptide of claim 1 wherein CM is ethylene diamine tetraacetic acid (EDTA), diethylene triamine pentaacetic acid (DTPA), cyclohexyl 1,2-diamine tetraacetic acid (CDTA), ethyleneglycol-O,O=-bis(2-aminoethyl)-N,N,N',N'-diacetic acid (HBED), triethylene tetraamine hexaacetic acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA), 1,4,7-triazacyclononane-N,N',N''-triacetic acid (NOTA), 1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid (TETA) or a compound of formula



wherein

PG is a sulfur protecting group selected from the group consisting of alkanoyl, arylcarbonyl, arylalkanoyl, acetamidomethyl, tetrahydropyranyl and tetrahydrofuranyl;

Y', Y'', and Y''' are hydrogen or oxygen with the proviso that at least one of them is an O;

R_1 and R_2 are hydrogen or alkyl (C_1-C_3);

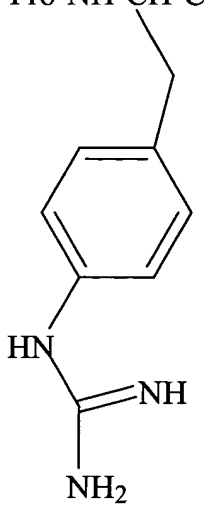
X = NH or S with the proviso that Y''' is hydrogen when X is S;

Z is PG if X is S; and

Z is hydroxyalkyl, aminoalkyl or carboxyalkyl.

7. The peptide of claim 1 wherein said peptide

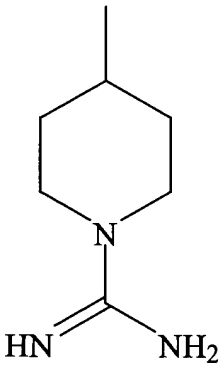
DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



I

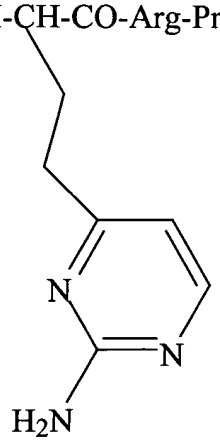
is

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



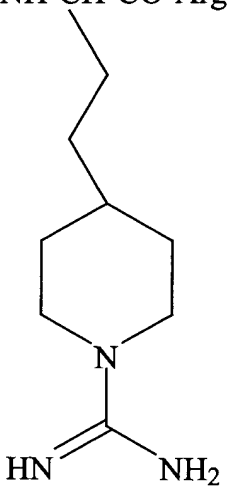
II

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



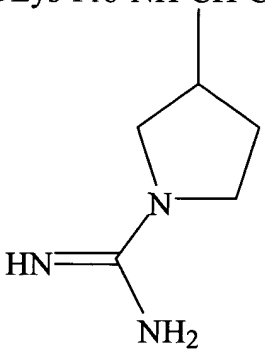
III

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



IV

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



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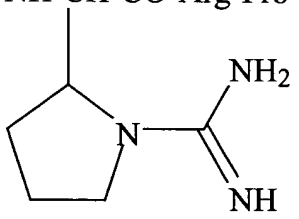
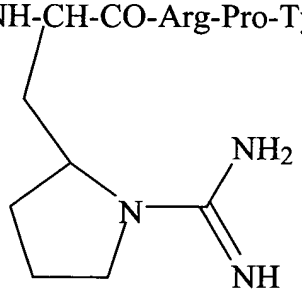
DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



VI

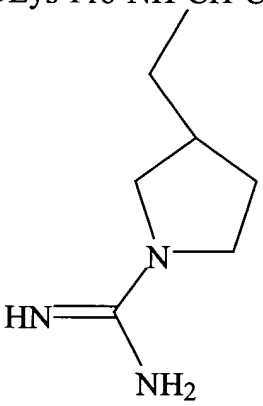
DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



VII

, or

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



VIII

8. A peptide of structure CM-R_3-$(CA)_n$-AA_1-AA_2-AA_3-AA_4-AA_5-AA_6-OH, wherein said peptide has a selective affinity for neurotensin receptors and wherein

CM is a chelating moiety or metal binding site;

R_3 is D-lysine, D-phenylalanine, any D-amino acid, glycine-glycine-glycine, Gly-Ser-Gly, Tyr-Glu-Asn, DTyr-Glu-Asn, Phe-Glu-Asn, DPhe-Glu-Asn, piperidinyl glycine, aminomethylcyclohexylalanine, other amino acid containing a cycloalkyl ring at the α- or

β-position with an amine group or an alkyl amino substituent either externally or as a part of the ring, or a spacer unit;

CA is a cyclic amino acid selected from the group consisting of proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or an alkyl amino substituent either externally or as a part of the ring;

n = 0, 1 or 2;

AA_1 is an amino acid which comprises a guanidino group and wherein the α-carbon is either L- or D-, with the proviso that AA_1 is not arginine;

AA_2 is arginine, lysine, piperidinylglycine, or other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the α-carbon, or AA_2 is an amino acid which comprises a guanidino group wherein the α-carbon is either L- or D-;

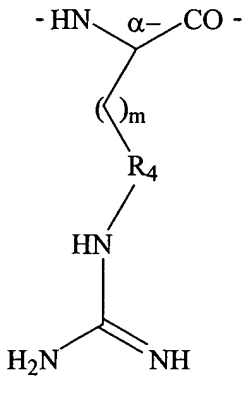
AA_3 is proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, or other amino acid containing a cycloalkyl ring at the α- or β-position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the α-carbon;

AA_4 is phenylalanine, tyrosine, an isomer of tyrosine, polyhydroxylated phenylalanine, or other aromatic amino acid wherein said amino acid can have the L- or D-configuration at the α-carbon;

AA_5 is t-butylglycine, 1-aminocyclohexylcarboxylic acid, cyclohexylglycine, trimethylsilylalanine, isoleucine, or other amino acid containing a branched or cyclic hydrocarbon substituent at the side chain at the α- or β-position, wherein the amino acid can have the L- or D-configuration at the α-carbon; and

AA_6 is cyclopropylalanine, cyclohexylalanine, t-butylalanine, leucine, or other amino acid containing a branched or cyclic hydrocarbon substituent at the side chain at the α- or β-position, wherein the amino acid can have the L- or D-configuration at the α-carbon.

9. The peptide of claim 8 wherein AA_1 is



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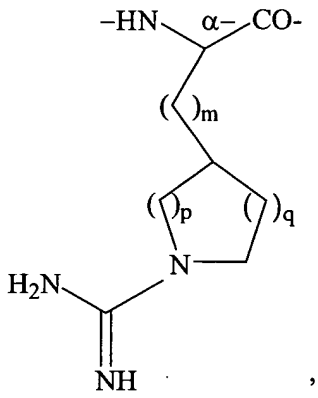

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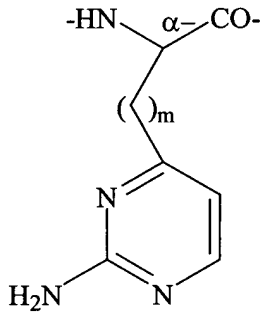


,

m = 0-6;

p = 1-7;

q = 1-7; and

R_4 is cycloalkyl C_3-C_{10}, phenyl, aralkyl, substituted phenyl or substituted aralkyl comprising an electron withdrawing or electron donating group with the proviso that said guanidino group is at a position different from said electron withdrawing or electron donating group.

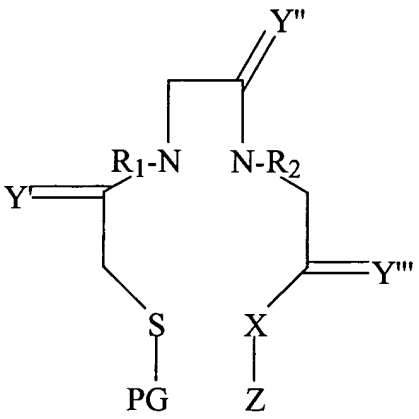
10. The peptide of claim 8 wherein said peptide is labeled with a radioisotope.

11. The peptide of claim 10 wherein said label is ^{99m}Tc, ^{203}Pb, ^{67}Ga, ^{111}In, ^{97}Ru, ^{62}Cu, ^{64}Cu, ^{186}Re, ^{188}Re, ^{90}Y, ^{121}Sn, ^{161}Tb, ^{153}Sm, ^{166}Ho, ^{105}Rh, ^{177}Lu or a radioactive halogen isotope.

12. The peptide of claim 11 wherein if said label is a metal then CM is a chelating group for said metal and if said label is a halogen then said halogen is bound to an aromatic ring.

13. The peptide of claim 8 wherein CM is ethylene diamine tetraacetic acid (EDTA), diethylene triamine pentaacetic acid (DTPA), cyclohexyl 1,2-diamine tetraacetic acid (CDTA), ethyleneglycol-O,O=-bis(2-aminoethyl)-N,N,N',N'-diacetic acid (HBED), triethylene tetraamine hexaacetic acid (TTHA), 1,4,7,10-tetraazacyclododecane-

N,N',N",N'"-tetraacetic acid (DOTA), 1,4,7-triazacyclononane-N,N',N"-triacetic acid (NOTA), 1,4,8,11-tetraazacyclotetradecane-N,N',N",N'"-tetraacetic acid (TETA) or a compound of formula



wherein

PG is a sulfur protecting group selected from the group consisting of alkanoyl, arylcarbonyl, arylalkanoyl, acetamidomethyl, tetrahydropyranyl and tetrahydrofuranyl;

Y', Y", and Y'" are hydrogen or oxygen with the proviso that at least one of them is an O;

R_1 and R_2 are hydrogen or alkyl (C_1-C_3);

X = NH or S with the proviso that Y'" is hydrogen when X is S;

Z is PG if X is S, and

Z is hydroxyalkyl, aminoalkyl or carboxyalkyl.

14. The peptide of claim 8 wherein said peptide is

DTPA-Arg-Arg-Pro-Tyr-Ile-Leu-OH (SEQ ID NO:3),

DTPA-DLys-Pro-Arg-(4-Gu)Phe-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-Ile-Leu-OH (Compound I),

DTPA-DLys-Pro-(4-Gu)Phe-(4-Gu)Phe-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-Arg-Aba(Apy)-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-Aba(Apy)-Arg-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-Aba(Apy)-Aba(Apy)-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound IX),

DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-Leu(Ψ-CH_2-NH)Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Ile-Leu-OH (Compound II),

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound X),

DTPA-DLys-Pro-Gly(PipAm)-Arg-(4-oxo)Pro-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-(2,6diMe)Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-mTyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro^R-OCO-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-PipGly-Pro-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-AzeCA-Tyr-tBuGly-Leu-OH,

DTPA-DLys-AzeCA-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Achc-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cpa-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cha-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-tBuAla-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-PipCA-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-DPipCA-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Chg-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Ile^R-OCO-Leu-OH,

DTPA-(Pip)Ala-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (SEQ ID NO:6),

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-DTyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Ala(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-homoAla(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,

DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-HA,

DTPA-PipGly-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound XI) (SEQ ID NO:4),

DTPA-*trans*-Cha(4-CH_2NH_2)-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound XII) (SEQ ID NO:5),

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound XIII),

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cha-OH (Compound XIV), or

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-tBuAla-OH (Compound XV).

15. A method for diagnosing a patient for a tumor by administering an effective amount of a peptide of claim 1.

16. The method of claim 15 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.

17. A method for diagnosing a patient for a tumor by administering an effective amount of a peptide of claim 8.

18. The method of claim 17 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.

19. A method for treating a patient for a tumor by administering an effective amount of a peptide of claim 1.

20. The method of claim 19 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.

21. A method for treating a patient for a tumor by administering an effective amount of a peptide of claim 8.

22. The method of claim 21 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.